June 3, 1953

Dr. R. E. Albert
U. S. Atomic Energy Commission
P. O. Box 30, Ansonia Station
New York City 23

Dear Doctor Albert:

I have sent you today the containers for the collection of samples of blood and urine referred to in our telephone conversation.

I suggest that you obtain two sets of samples at intervals of approximately one month. Instructions for obtaining the samples accompany the containers. I wish to supplement them by saying (1) that the duplicate samples of blood, obtained at the same time, are for the purpose of checking against the possibility of contamination; and (2) that two "spot" samples of urine obtained from two separate voidings at different times in the same day help to equalize the physiological variability of the urinary excretion of lead and so to contribute to the precision of the interpretation. The information from all of these analyses on the two separate occasions, when combined with your determinations of the concentration of radioactive lead in the blood on the two occasions should enable us to arrive at some fairly definite idea of the concentration of radioactive lead in the skeleton, if the amounts are not too small to be of significance. I suspect that the latter will be the case. (The determinations on the blood are greatly to be preferred over those on the urine.)

My remarks concerning the relationship between the lead content of the blood and/or the urine and the lead content of the body, including the skeleton, may have sounded a bit dogmatic, especially with relation to the book of Canterow and Trumper. In explanation, let me say that I was being brief and to the point on the telephone. The facts are that there was no satisfactory basis for any such interpretation until our experiments were done on the response of normal healthy persons to the ingestion and inhalation of known quantities of lead over definite periods of time. It was for this reason that these elaborate and costly experiments were undertaken. The results have never been written up in detail and have never been interpreted in the relationship with which you are concerned. In fact nothing has been published yet on the inhalation experiments, which are now in progress. They are the most revealing in a number of respects, since they deal with the total intake and output of lead. Moreover, the authors of the book to which you referred never achieved the faintest glimmer of understanding of the physiological pattern of the processes involved in the general lead metabolism under a

variety of conditions, but rather they confused the matter with their uncritical review of the literature.

I send you two reprints which will illustrate the methods and the general facts obtained in the ingestion experiments. Unfortunately an intermediate article is no longer available in reprint form. It can be found in the Journal of Industrial Hygiene and Toxicology, 25:71,1943. It gives the type of information in which you are interested, but not in full. With these articles at hand, you will see why I have said that the time factor is one of the items in the equation employed to relate lead in the body to lead in the blood or excreta. Unfortunately, in the present state of our knowledge, the time factor cannot be given a precise or definite mathematical expression, for the reason that the intrinsic error of the entire experimental procedure, while small in the absolute, is large in relation to the overall quantities of lead involved in the day to day process. This means that the quantities set down are the result of the summation or the statistical analysis of values obtained over some period of time, and while time enters into the calculation in either instance it is used to visualize a trend and it, itself, is obscured in the process.

Certain features of the observation on the ingestion of lead should be emphasized in relation to your specific problem. (1) Lead ingested in one dose, regardless of its form, is but poorly absorbed. Most of it (more than 90 per cent) passes through the alimentary tract unabsorbed and since a large dose, to the extent that it is absorbed, would induce an increase in alimentary parystalsis, it would pass the tract with abnormal speed and so be even more scantily absorbed.

(2) Lead absorbed from the alimentary tract will go in relatively large quantity to the liver, from which it is readily excreted via the alimentary tract, thus reducing rapidly, the quantity available for general distribution in the other tissues, including the skeleton. correspondingly
(3) The result of a short period of rapid lead absorption is a / high rate of lead excretion (renal, alimentary and, if sweating, cutaneous) for a roughly corresponding period of time. Under these conditions there is only a minute amount of distribution into the skeleton. If the dose is small or moderate, the skeletal deposition is small, often too small to measure by chemical means.

(4) Lead distributed into the skeleton is not deposited in inert form, but is lost from the skeleton in accordance with a normal process of equilibrium with the other tissues. That which is most recently absorbed is most readily available for release. For the latter reason the lead which reached the skeleton as the consequence of the ingestion of one dose of lead would be the first to leave the skeleton.

(5) The failure of the patient, in this instance, to develop alimentary symptoms means that the dose taken was small. The appearance of symptoms of some type some days or weeks later, in the absence of any early symptoms, merely means that the complaints had no origin in the ingestion of lead. Perhaps the patient was the victim of anxiety, or perhaps he (or she) was overtaken by some incidental illness.

I shall be glad to do what I can to solve the problem which you present, but I may say that in my present opinion there is very little reason for any anxiety about this person.

Sincerely yours,

Robert A. Kehoe, M. D.

RAK ef

Enc.

Experimental Studies on the Ingestion of Lead Compounds - Kehoe, Cholak, Hubbard, Bambach, McNary and Story
Exposure to Lead - Kehoe
The Plasma-cell Partition of Blood Lead - Bambach, Kehoe and Logan

P.S. A reprint on the lead in the blood is also being sent.

I might comment on the fact that after the lapse of sufficient time (5 to 10 days) the great bulk of the lead (inorganic) that is absorbed and retained, following the absorption of a single large or moderate or small dose, or a series of such doses, in excess of the normal daily intake of approximately one third of a milligram, will be found in the skeleton (well over 90 per cent). This excess of retention, over that which is found normally in the body of the adult, is lost gradually in part or in whole, so that the lead content of the body tends to reach its normal level. In the skeleton this normal level, in terms of concentration, approximates 1 to 2 mg. of lead (Pb) per 100 grams of fresh bone. There is some slight difference between the long bones and the flat bones in this regard, but this difference would probably be insignificant, from the aspect of physiological effects. Certainly it would be of less significance than the variation in the total lead content of adult individuals - a difference which is based largely, it seems, on the daily level of lead intake, which in turn varies with the dietary habits of the individual, with respect to the quantity and types of blood consumed.

R.A.K.